

# ST. BARTHOLOMEW'S HOSPITAL JOURNAL



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## EDITORIAL

Parkinson's Law states that work expands to fill the time available for its completion ; that is to say, if you have all afternoon in which to write two postcards, then it will take you all afternoon to write them ! The corollary of Parkinson's Law is a much older observation of human nature, namely that it is always the people with most to do who seem able to fit in something more.

People may well wonder how it is that a busy surgeon is able to find enough time to undertake the office of Dean of a Medical College, especially one that has a full programme of rebuilding and expansion. Nevertheless, our Dean has found time to undertake yet one more task, namely the "open days" to be held on June 10th and 11th.

The afternoon of June 10th is intended as an "open day" for the parents of preclinical students only (this restriction being based purely on the number of people for whom the administration can cater) and on June 11th, old Bart's students are invited to return to look over the hospital and to attend a series of clinical demonstrations. The number of persons who can attend the demonstrations is limited, and early application is advised.

These two "open days" have involved a lot of extra work for the Dean and his staff, and it is to be hoped that they will be well supported so that they achieve the success which they deserve.

While still on the subject of Parkinson's Law, people have been heard of late to make two diverse complaints which nevertheless spring from a common cause. Some have found parts of the clinical course dull as their time is not fully occupied, others have grumbled that certain specialist aspects of medicine and surgery are not catered for in the organisation of the clinical course. These people must have been allowing trivia to completely fill the time available for their completion, if they have not seen that the remedy lies in their own hands.

The Dean has recently called attention to the fact that ward rounds are open to all students in the hospital and not restricted to members of the firm. Furthermore, most of the specialised out-patient clinics are prepared to undertake teaching and students should make their own arrangements with the chiefs concerned. In future, any aspiring cardiologists, urologists or endocrinologists should make their own arrangements and not wait to be spoon fed. The facilities are there.

It seems a pity that there is no organised system of intelligence whereby the students of this hospital might learn from their colleagues elsewhere who are the outstanding teachers in the other London hospitals. We are fortunate in having a high proportion of excellent teachers and lecturers on the staff of this hospital, yet contact with outside ideas

and other men of outstanding ability is always stimulating, and we would surely benefit from occasional visits to other hospitals in the same way as their students would benefit from visits to us. Such student enterprises

seem to have been fairly common in pre-war days, and if such activities are no longer considered desirable from the official point of view, perhaps an official exchange of lecturers could be arranged.

### New Treasurer

We would like to extend a hearty welcome to Mr. M. W. Perrin, the new Treasurer of the Hospital, who succeeds Sir George Aylwen. Sir George, who has held the position since 1937, was formerly a most distinguished figure in the City, and was Lord Mayor of London for the year 1948-49; he is, in addition, President of the Medical College and a member of the Management Committee of King Edward's Hospital Fund for London.

Mr. Perrin, who is fifty-five, is the Chairman of the Wellcome Foundation Ltd., and of the Postgraduate Institute of Cardiology. Educated at Winchester and New College, Oxford, he has studied also in Toronto and Amsterdam. Mr. Perrin was Deputy Controller of Atomic Energy (Technical Policy) at the Ministry of Supply from 1946-51, and Research Adviser to I.C.I. 1951-52. We wish him a successful tenure of office.

### Dr. M. J. Blunt

The good wishes of the Medical College will go with Dr. M. J. Blunt on his appointment to the foundation Chair of Anatomy in the University of New South Wales.

Dr. Blunt came to Bart's in October 1955, from the Royal Free Hospital, bringing with him interests in the blood supply of nerves, and women's hockey. He has been a most valued teacher, colleague and prandial connoisseur, and will be greatly missed from the Anatomy Department. Before leaving, he was initiated into the superior habit of snuff-taking, and this will serve to refresh his memory of Charterhouse.

The University of New South Wales received its charter in 1958, and has Faculties of Science and Technology already in existence. The Faculty of Medicine is about to be established, and Dr. Blunt will have the exciting task of planning and supervising the erection of its Anatomy Department, in which task his natural gifts of organisation will have full scope.

C.J.P.

It was with great regret that on March 5th we said goodbye to Dr. Blunt. On March 20th, Dr. Blunt sailed for Australia to take up his new appointment and with his departure the Hockey Club loses one of its most keen and loyal supporters. For four years Dr. Blunt has followed our fortunes with interest and, together with Mrs. Blunt and their daughter Jackie, has cheered us from the sideline many, many times. All present members of the Club and very many past members will wish to join me in thanking them for their kindness and enthusiasm, and to wish them every success and happiness in their new life in Australia.

E.K.

### News in Brief

Mr. G. W. Taylor has been appointed to the University of London Chair of Surgery tenable at the Medical College of St. Bartholomew's Hospital.

Mr. C. Naunton Morgan was made a Honorary Fellow of the American College of Surgeons at their annual meeting in Atlantic City.

Mr. D. A. Macfarlane, M.Ch., F.R.C.S., Surgical Tutor and Casualty Surgeon, has been appointed Consultant Surgeon to the Chelsea Group of Hospitals.

Mr. R. S. J. Clarke, M.D., M.B., B.Ch., B.A.O., B.Sc., has been appointed Lecturer in Physiology and Tutor in Anaesthetics.

Dr. D. W. Gould, B.Sc., M.R.C.S., L.R.C.P., D.T.M.H., has been appointed Lecturer in Physiology.

Dr. R. E. Watts was successful in the University of London examination for the degree of M.D. held in February.

The Sailing Club Regatta will be held at Burnham-on-Crouch from May 18th to 20th. All are welcome to attend.

In the March issue of the *Practitioner*, Dr. A. W. Spence writes on the "Endocrinological Problems of Adolescence." Dr. C. Nicol contributes a paper on "Homosexuality and Venereal Disease" to the same issue.

Dr. G. Simon addressed the North-Western Thoracic Society on March 10th on the subject, "Radiological Changes in Heart Disease."

The following lectures were given by Bart's men at the Royal College of Surgeons during the month of March:—

Thursday, 3rd, 5.30 p.m. Dr. R. B. MacKenna: The dermatological aspect of certain of the diseases of the mouth and ear (Otolaryngology lecture).

Thursday, 24th, 5 p.m. Dr. A. G. Stansfeld: Necrotising arteritis (Erasmus Wilson Demonstration).

Wednesday, 30th, 5 p.m. Prof. J. P. Griffiths: The dissemination of cancer cells during operative procedures (Hunterian Lecture).

### Antibiotics

Professor Garrod has recently published a report of some work with a new oral penicillin, the potassium salt of 6-(alpha-phenoxypropionamido) penicillanic acid. This has been marketed under the name "broxil." The activity of this penicillin against penicillin-resistant staphylococci in a form of test which measures resistance to penicillinase shows that it is generally more effective than both penicillin V and G.

The latest issue of the *British Medical Bulletin*, "Antibiotics in Medicine," is edited by Professor Garrod. Now that there is such a wide choice of antibiotics available, great care is needed in their use if the formation of resistant strains is to be minimised. Some advice given by Professor Garrod and Dr. Scowen in the *Bulletin* is that:—"Each case must be judged on its merits, but if these are deliberately assessed, and if treatment has an explicit rational basis, really indiscriminate use will thereby be excluded."

### Abernethian Society

The Abernethian Society hooked a large and topical fish on March 3rd when Mr. A. Dickson Wright, of St. Mary's Hospital, came to proclaim his policy of "Keeping the Patient in Ignorance." The case was presented at length, and with admirable skill, and a wealth of corroborative case histories. Hypertension and cancer were put on the secret list, with reasons for their choice. Tales of heroism and suicide were successively recounted to illustrate the disastrous taste of the apple of knowledge in the welfare Garden of Eden. Once his patients had eaten of it, Mr. Dickson Wright found it beyond his power to help them.

At the beginning rows of ethical gentlemen sat hatchet-faced and eager for the blood sport of question time, but before the end their stamina was exhausted. The clock (obvious only to the audience, unlike that in the clinical lecture theatre) called to dinner. The questions were emasculated and the answers authoritative. Tray in hand in the dinner queue, we knew that our fish had got away, line and all.

D.G.M.

Dr. C. H. Andrewes, Deputy Director of the National Institute of Medical Research, spoke to the society on March 17th. Because Dr. Andrewes was once a President of the Abernethian Society, and in view of the recent progress which had been made in the study of colds and influenza, this was a particularly interesting meeting.

He started his talk by describing the early work which was done on the transmission of influenza. The ferret was found to be a very important animal in the experiments and was particularly susceptible to influenza. The study of cross infection and immunity was made very difficult because of the marked "antigenic drift" which the influenza virus exhibits. The technique of inoculating eggs with the virus has helped work greatly and it should be possible in theory now to predict the spread of an epidemic and check its advance by inoculation.

The common cold has many features which make it as difficult to study as influenza. In addition to the difficulty of transmitting the virus and clinically estimating whether the subject has a cold, there is still the great difficulty of growing it. Recent work has led to a method by which

the virus can now be grown successfully in human embryonic tissue. First lung was used and now kidney seems to be the tissue of choice. Perhaps this is because kidney grows epithelial tissue so readily.

Dr. Andrewes made one or two speculations about the outcome of the present work. Certainly a very important step has now been made by the new culture techniques. However before we start to think of producing anything like a live attenuated strain for a vaccine there is a lot of work to be done in the study of the natural history of the disease and in starting a reference laboratory of the different viruses which are continually being found.

### Film Society

On Monday, April 25th, the Film Society is showing "Strange Incident" with "His Marriage Wow" and "Persian Story."

"Strange Incident," a Western, starring Henry Fonda, was originally entitled "The Oxbow Incident" in the U.S.A. It was refused general release by the major distributors in this country after the war, because in its novel and intelligent use of shadows and arrangement, it had pulled too far ahead of the mass audience, in the same way as "Citizen Kane." The film is a devastating portrayal of mob hysteria, culminating in a lawless lynching.

"Persian Story" is a BP film about the development of Persia's natural wealth; and "His Marriage Wow" is a Harry Langdon comedy ending with the inevitable car chase.

As regular members will know, the quality of the sound has been considerably improved.

A.P.

### The Christian Union

There have been two open meetings this term, and it was good to have such a large attendance, particularly at the first, on Tuesday, January 26th, when Lieut.-Gen. Sir Arthur Smith, K.C.B., K.B.E., D.S.O., spoke on "A Purpose in Life." From his own experience he showed clearly how a personal relationship with Christ gave him a real purpose in life.

On Tuesday, March 8th, Mr. Morgan Williams, F.R.C.S., gave a most thought-provoking address on the "Reality of Christianity." After pointing out that there

are hypocrites in every sincere body of people or group of society, he went on to discuss the reality of true Christianity. He showed that there is factual evidence for the truth of the Bible, and quoted a barrister who studied in an attempt to disprove the Resurrection of Christ, and was ultimately convinced of its truth. He then pointed out the practical influence of Christianity through the ages; and the experience of men of God, such as George Muller, who ran an orphanage in Bristol for 2,000 children. He never issued an appeal, but every need was met, for he prayed earnestly over his requirements, and then trusted that God would answer. For example, on occasions Bristol merchants felt compelled, on waking during the night, to arise, load a carriage with food and then to take it to the home, in order that the children might have food for breakfast. Thus did Muller show the practical reality and power of prayer.

Mr. Williams then closed by telling of his own experience of Christianity and suggesting that we find out and test its reality for ourselves.

### Students' Union Council

At a meeting held on March 9th it was decided to allow the sale of *Sennet* within the Medical College. The Council agreed that there was no point in discriminating against *Sennet*, and as there are people prepared to distribute this paper, its sale will be permitted in the future.

The Film Society applied for official backing from the Students' Union for the making of a film of student activities at the Hospital. The film would be of 30-40 minutes' duration and would be suitable for showing to freshmen. The council approved the scheme in principle but, before promising financial support, asked the Film Society to go ahead with a pilot scheme, a ten minute film, showing Saturday afternoon activities.

The Council approved the official formation of a Ladies' Squash Club.

### Bart's-Cambridge Club

The annual dinner of the Bart's-Cambridge Club was held at the Connaught Rooms on Friday, March 25th, with Dr. Brewer in the Chair. An excellent dinner was served, which prepared the way for the speeches which followed. Of these, probably the most illuminating was Dr. Abercrombie's speech

proposing the health of the Chairman ! It was a pity that more junior members of the hospital did not avail themselves of the subsidy offered, as this was a most successful occasion, for which our thanks are due to the two Secretaries.

Dr. R. A. Shooter would be glad if all members of the Club would keep him notified of their various changes of address. His records are most lacking in this respect for members who are in their first five years after leaving the hospital.

#### Twelfth Decennial Club (1925-1935)

The Annual Dinner of the Twelfth Decennial Club is to be held at the Naval and Military Club, 94 Piccadilly, W.1, on Friday, May 13th. Chairman, Dr. Kenneth Latter.

Will any member who does not receive notification, or any eligible non-member who would like to attend the Dinner, please get in touch with W. D. Coltart at 58 Harley House, N.W.1.

#### Wessex Rahere Club

The Spring Dinner of the above Club will take place at the White Hart Hotel, Salisbury, on Saturday, April 30th. It is hoped that, as usual, a member of the Staff will be present as Guest of Honour. Membership of the club is open to all Bart's men practising in the West Country. Further details will be circulated to members and to any other Bart's men who are interested and who will get in touch with the Hon. Secretary, Mr. A. Daunt Bateman, 11 The Circus, Bath.

#### Infant Feeding

On March 8th, the firm of Trufood Ltd. gave a press preview of their new film, "Tailored for Timothy" at the British Council Cinema. Designed for showing to pupil midwives, mothercraft classes and antenatal clinics, this well made film, which runs for about thirty-five minutes, sets out to reassure the mother who is unable to breast feed her baby. It shows how cow's milk can be specially prepared (mainly by the removal of indigestible protein and the addition of vitamins) to provide a satisfactory substitute for mother's milk. The audience is shown factory shots of this work in progress at the Trufood Creamery, and the

techniques of bottle feeding are well illustrated.

The film has been made in close association with the Royal College of Midwives and the staff of St. Thomas's Hospital, where many of the live sequences were filmed. The film is available free to those interested, and copies may be ordered either from Trufood Ltd., at 113 Newington Causeway, S.E.1, or through the Company's representatives.

#### Film Festival

The first British Medical Film Festival will be held in London on July 5th to 7th inclusive. It is intended that the Festival, which is organised by the *British Journal of Clinical Practice*, shall become an annual event at which practising, teaching, nursing and student members of the profession will have the opportunity to see some of the best of the many fine medical films made in this country.

Fifteen films will be shown at the Festival, covering general medicine (including paediatrics), surgery (general and specialised), and obstetrics and gynaecology. The films will be judged by a panel appointed by the Editorial Board of the *British Journal of Clinical Practice*, and all films shown at the Festival will be awarded a Medal of Merit.

Further details, including the conditions of entry of films, can be obtained from the B.J.C.P. Offices at 171 New Bond Street, London, W.1.



Miss E. Knight, captain of the victorious Ladies' Hockey Team, is chaired from the field after the Cup Final

### Building at Charterhouse

The University Grants' Commission and the University of London have approved the erection of the Library block on the site of the old Great Hall at Charterhouse. The hiatus due to the lack of £26,000 ready cash (mentioned in the Dean's report—January issue of the *Journal*) has been closed, and it is hoped that work will be started on the site this year. The cost of the building will, however, absorb the whole of the Medical College's reserves, and it is hoped to raise at least £25,000 by private subscription to cover the cost of the Library itself. A Research and Development Fund has been opened to enable the College to rebuild its Endowment Fund and plan for future extensions.

### Cleaning of Hogarth Murals

Work has been in progress since the beginning of February on the cleaning and restoration of the Hogarth paintings on the Grand Staircase leading to the Great Hall. These pictures were painted by Hogarth (1697-1764) in memory of his birth near the Hospital.

Mr. Freeman, of Albemarle Street, and his assistant, Mr. Ellison, have removed all the old varnish and have thoroughly cleaned the pictures. In the course of their work they have removed some sepia over-painting which they think must have been added by restorers in the last century who did not fully appreciate the meaning of the pictures. As a result of this, the grisailles (monochrome paintings below the main subjects showing Rahere's dream, the foundation of the hospital and a patient on a stretcher being received in the cloisters) are now seen in their true colour.

The restorers are now revarnishing the pictures and touching up areas of minor damage, joins in the canvas and places where previous over cleaning, when the paint was newer and cleaning techniques less refined, have left the image rather thin.

During the cleaning process the restorers have found evidence that Hogarth changed the design of his murals even while he was working on them; for example, the leg of a cherub has been discovered appearing from behind a tree. Such over-painted remnants of earlier design are known as pentimentos.

These unique canvases are in fine condition, having escaped any major damage and, as Mr. Ellison pointed out, there is no evidence of cupping of the paint or stretcher marks.

The brushwork is of a high standard and compares well with Hogarth's easel paintings.

It is to be hoped that after all the hard work which has been expended on these paintings, a consultant electrician will be called in to arrange for their proper illumination.

### Renovations

On Monday, March 7th, workmen started the systematic removal of furniture and fittings from the Pathology Classroom and the adjoining lecture theatre. Both are to undergo a complete refit. The lecture theatre will contain an increased number of seats of a more modern and comfortable design and the classroom is to be laid out on one level only with the benches facing the doors leading into the Pathology Department. It is expected that the work will be completed by November and, in the meantime, practical classes are being held in the museum.

The design of the old Classroom, with its close resemblance to a court of law, is attributed to the late Sir Bernard Spilsbury, the eminent pathologist.

Sir Bernard Spilsbury was born in 1877 in the town of Leamington, where his father, James, had a prosperous wholesale pharmaceutical business. During his youth he was subject to the marked Non-Conformist influences which prevailed in the Midlands— influences, which though narrow in their outlook, produced great men such as Lister, Kelvin and Crookes. It may have been these influences which helped to form his attitude towards criminal abortion and led to his vigorous investigation of such cases.

James Spilsbury was a restless man, moving about the country as the interests of his business dictated, and Bernard was sent to Leamington School, University College School, Manchester Grammar School and Owen's College, successively.

With general practice in view, Bernard was sent to Magdalen College, Oxford (where he had rooms overlooking the Deer Park), to do his preclinical work. On coming down from Oxford he went to St. Mary's Hospital where he met Drs. A. P. Luff, W. Willcox and A. J. Pepper—at that time, probably the three most eminent forensic pathologists in the country. Under their tutelage his bent for pathology and interest in medico-legal work rapidly developed. Indeed, his profound interest in morbid anatomy caused him to

devote so much time to that subject that he delayed qualification, and it was not until 1904 that he gained M.R.C.S., L.R.C.P. He did his first post mortem in January, 1905, and within two years of qualifying was giving evidence in ten London Coroner's Courts.

The Crippen case in 1910 was the first of many in which he was to play a leading role, and in which he was to become known to the public, in Lord Darling's words, as "that incomparable witness." The long list of his cases is the history of crime between 1910 and the Second World War, and includes, apart from the Crippen trial, the Seddon case, the Brides in the Bath and the Armstrong case.

In November, 1920, a quarrel with a colleague led to his resignation from the staff of St. Mary's Hospital and, later in the year, he came to Bart's as Lecturer in Morbid Anatomy. Here he was as busy as ever, and was soon working more than twelve hours a day. He gave three morbid anatomy lectures a week as well as a special course in forensic medicine, and his morbid anatomy demonstrations were always popular. In July, 1923, at the St. Bartholomew's Fair, he was photographed in an undignified position for the first and probably the only time in his life, for having been waylaid by a group of students, he was clapped in the stocks, where Lady Spilsbury found him some time later !\*

Sir Bernard suffered a stroke in 1940, and from that time his health slowly and almost unperceptibly declined until his death in 1947.

"... it has been said, he raised the giving of professional evidence from a suspect and controversial status to an honourable and exact plane."\*

### Fifty Years Ago

At the time of the Franco-Prussian war we are told by Henry Rundle, F.R.C.S., how "a great wave of excitement and concern swept over England, followed by an outburst of sympathy." In his article he tells of how a medical expedition went out from England to help the sick and wounded of both sides. This mission, he recalls, started by an appeal to *The Times* and led to the formation of the Red Cross Society.

'Our neighbours were on the eve of a

\* Bernard Spilsbury : His Life and Cases. D. G. Browne and E. V. Tullet. Harrap.

fight of gigantic magnitude, and as the fumes and aftermath of our recent experience of war still lingered with us, we knew only too well the hardships and perils of the strife upon which our neighbours were embarking. A letter appeared in *The Times* of July 22nd from Col. Lloyd Lindsay (afterwards Lord Wantage), asking for aid for the sick and wounded in their hour of need, and a public meeting was held in Willis's rooms on August 4th in support of this object.

It is difficult to say how much of the inevitable horrors and misery of the war were mitigated by the humanity and generosity of Col. Lloyd Lindsay. The Red Cross Society, which owes its existence to him, is a permanent memorial to the nobility and goodness of his life and a confirmation of the belief :—

"... that somehow good  
Will be the final goal of ill."

An office of the society was opened at 2, St. Martin's Place.' It was evidently not long before the organisation began its work, for 'The Pall Mall Gazette' of August 11th, 1870, contained the following paragraph : "The Committee of the Society for aiding the sick and wounded in the French and Prussian Armies, after communicating with the committees formed in Paris and Berlin, and learning from them in what manner the most effectual assistance could be given, have sent out six surgeons to the seat of war, who will work under the Red Cross Society, and receive their instructions from the president at Berlin and at Paris. The Society will defray the expenses of these gentlemen, but their services will be in other respects gratuitous. The Society has also sent £500 to Paris and a similar sum to Berlin."

We all crossed the Channel together, and my readers can imagine the hopes and fears, the plans and ambitions that filled our minds on such a journey. We were all eager to get to the front, impatient to know what the future held in store for us. It was a crossing from the routine of things familiar into the darkness of the unknown. Everything seemed vague and adventurous, except the fact that there would be work to be done, and plenty of it, and each of us was determined to do our utmost for the honour of our country, our profession and those who had chosen us.

On the day after our arrival in Berlin the Crown Princess of Prussia very graciously received us . . . even the Royal Palace at

Potsdam had been placed at the disposal of the authorities for the storage of articles for the use of the sick.

Before we could begin active service we had to obtain from the military authorities our war passport, or "Legitimations Schein," and badges bearing the distinctive symbol of the red cross. Once in possession of these we were free to join the army before Metz.

Many churches in the district had been utilised for the reception of the wounded. There was urgent need of a reserve hospital and the Hessian War officers placed at our disposal a drill ground on the outskirts of the town. Four large well equipped pavilions were erected. Provision was made for 120 beds, which were ultimately increased to 250. In this hospital 926 sick or wounded soldiers were treated. Many of them were cases of enteric and dysentery, but we saw and did much good surgical work.

This, the only hospital in Germany under British management, was founded under the auspices of the Princess Louise of Hesse-Darmstadt (Princess Alice of England), and was known as Alice Hospital.

#### World Refugee Year

As this is World Refugee Year, the Students' Union has decided to support the University Carnival. A most successful collection of jumble has already been made and our beer drinking team reached the final of the contest (see below). More events are to take place in the near future, culminating in a Fête on May 14th, details of which will be posted later. The Carnival procession will be the climax of the festivities, and it is hoped that the Hospital will enter a float on the theme "A Penny for Them." Offers of assistance or ideas for this would be of greatest value, and anybody interested should contact the Publicity Officer (J. U. Watson).

The collection organised by the B.M.S.A. representative has so far realised £70.

#### Beer Drinking Contest

With the third best time in the eliminating round, Bart's entered the final confident that time spent in practice would be rewarded! Unhappily it was not the team's good night, and their time of 88.1 seconds (three pints per man) was twenty seconds slower than the Guy's team, who carried off the very handsome pin of ale provided by Messrs. Courage and Barclay. In the reeking atmosphere of

the New Merlin Cave the performance of the immaculately attired Guy's men had to be seen to be believed, and they are to be congratulated on upholding the honour of the profession against all comers.

The Bart's times were as follows:—

- R. Bergel, 18.5 seconds
- C. Burke, 18.4 seconds
- C. Craggs, 22.8 seconds
- M. Ernst, 28.4 seconds

Times are for three individually timed pints.

#### Symposium on Rheumatic Diseases

It appears that the word "Rheumatism" was coined in the reign of Queen Elizabeth I, but until some twenty-five years ago little work was done in this field. No adequate classification of the various syndromes which come under the heading "rheumatism" was attempted and consequently little science could be applied to the subject.

Just before the last war, the Royal College of Physicians evolved a scheme of nomenclature which forms the basis of the clinical terminology which is used today. "Once clinicians were able to differentiate the various types of rheumatism and diagnose them on the basis of a common nomenclature, research became possible."\*

In 1936, the late Lord Horder founded the Empire Rheumatism Council to promote interest in the rheumatic diseases among doctors and lay-people alike. The Council also aimed to give financial support to research in this field, and to help in improving methods and facilities for treatment. Amongst other achievements the Council has now established two professorial chairs, endowed research work by its Fellows in eight British universities and has been able to finance a number of Travelling Fellowships.

The present symposium illustrates well how far our ideas on the aetiology and treatment of rheumatic disease have advanced in recent years, and we would like to thank contributors for all the hard work they have put into it.

General Practitioners and others who wish to keep abreast of developments in the field of rheumatology might be interested in the excellent series of Reports issued and obtainable from the Empire Rheumatism Council, Faraday House, Charing Cross Road, London, W.C.2.

\* Reports on Rheumatic Diseases, No. 1 (January, 1959). Empire Rheumatism Council.

### Supplement

In order to help those who have a spare morning or afternoon to know what is going on in the hospital, the centre page pull-out supplement contains lists of ward rounds and out-patient clinics. The Editorial staff and Appointments Bureau have done their best to ensure that these are up to date and accurate. We would, however, like to apologise for any mistakes which have eluded us.

### "Charley's Aunt"

"Charley's Aunt" was first produced at the Royalty Theatre, London, in December, 1892. Its original London run lasted for four years. Since then it has been revised on numerous occasions, and has been filmed very successfully. It is an amusing play, and is so constructed as to be an easy production for amateurs to achieve a high standard.

The Dramatic Society has been criticised in the past for lack of originality in its choice of play, yet when they have stepped outside the libraries of "drawing-room comedy" they have been criticised for biting off more than they can chew. Much praise should be given to them for putting on this play in the three weeks which were available for rehearsing, learning of parts (some of which are long) and getting programmes printed and tickets sold. Quite a lot of energy and time was expended to produce the two nights of theatre, which the audience enjoyed at the Cripplegate on February 22nd and 23rd.

Amateur actors often believe that the main object of their society is that they, themselves, should enjoy the production, and yet it is very rarely that the audience is not expected to pay to watch them doing it. In fact, the first principle of amateur and professional theatre alike must be to give the audience their money's worth, even if that calls for a great deal of hard work for the cast and the back-stage staff. Ultimately, the enjoyment of the final product is greatest for audience and cast alike, for in the theatre the maxim that the more one puts into a thing, the more one gets out of it, is most certainly upheld.

In this production the audience, which was made up mainly of personnel of the hospital, thoroughly enjoyed viewing a show in which the cast were so obviously enjoying themselves as well.

All would-be actors should remember that when stage movements and actions are

included in the script (and a great many are in this play) then they are usually the movements which were made in the original production and are only to serve as a guide to the action, and must be adapted to the stage and to the individual actors. It is useless for an actor to make a gesture just because it is noted in the script; he must understand the reason for it, or not make it at all. Too often did we see unnecessary or awkward changes of position spoiling the stage picture. Some of the actors had a nasty habit of fidgeting when someone else was speaking, which is very distracting to the audience. It is easy to ruin another player's best lines by one false gesture at a crucial moment.

David Gibson, as John Chesney, gave an excellent performance; he has a fine command of the stage and convinced at least one member of the audience that he was the dominant character—which is just what the author wanted.

Brasset—the manservant—was played by Basil Middleton, in a plain, unmoved manner, which well suited the part, and Charley Wikeham, portrayed by Mike Thomas, was rather too awkward in his shyness, and lacked the charm which this part called for, nevertheless, he improved as the evening progressed and he gained confidence.

Lord Fancourt Babberly is a very difficult character to portray. Those who have seen the play will recall that it is he who, dressed as an elderly woman, impersonates Charley's Aunt, in order to provide a chaperone for two young ladies. The problem for the actor is to choose a happy medium between clowning and being over serious. Undoubtedly, this is a frolic and the trend should be towards clowning. Nick Roles managed to select almost the degree required, although there were moments when we witnessed a little too much horse play.

The two young ladies, Kitty Verdun and Amy Spetigue, were played by Janice Swallow and Diane Tobitt. Miss Tobitt suffered a little from inaudibility. Miss Swallow acted and re-acted splendidly in her scene with David Gibson. Love making, even of a Victorian kind, is not the easiest thing to portray on the stage.

John Creightmore—surely Bart's will miss him greatly when he leaves later this year—was Colonel Sir Francis Chesney, and Donald Gau was Stephen Spetigue—the bad tem-

pered, pompous, yet charming solicitor.

Wendy Roles was a high spirited Ela Delahay but made one wonder, on more than one occasion whether she understood the meaning of the words she was speaking, as the intonation of her voice seemed wrong.

The real Charley's Aunt, Donna Lucia D'Alvadorez, from Brazil—"where the nuts come from"—Vanessa Jones, looked every inch the part, and acted extremely well. She held the stage whenever it was necessary, but never intruded when it was not.

The stage staff worked much harder than many believe. Stage management was undertaken by John Newton, properties by Gillian Turner and Judy Darmady looked after the costumes, which were very pleasing, except for Nick Roles' "Aunt" costume, which should have been much smarter—this looked rather like a piece of blackout material left over from the last war. Grateful thanks are due to "Bert" junior for the excellent make-up.

The stage lighting—there was no acknowledgment on the programme—was disappointing. Characters walked from light to shade in at least four different places across the stage. Surely the Cripplegate Theatre is equipped to do better than this? The play

was well produced in a short time by Trevor Robinson. The Dramatic Society must ensure that there is longer to rehearse in future, and properly advertised auditions would be welcome. The choice of future plays is problematic. Other hospitals produce such plays as "The Crucible," but while this is praise-worthy, is it good box-office? In this day and age when few arts thrive without a subsidy, the Students' Union should be prepared to cover the Dramatic Society's losses. Looking further ahead, let us hope that the Students' Union building in Charterhouse Square will include a properly equipped stage.

C.A.H.

#### Errata

November, 1959 (Vol. LXIII, No. 11): Mr. S. H. C. Clarke's new address is 105 The Drive, Hove, 4, Sussex, not 104.

February, 1960 (Vol. LXIV, No. 2): p. 34, para 4, for Hole read Place.

The Editor regrets any inconvenience caused by these errors.

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## Historical Diagnosis

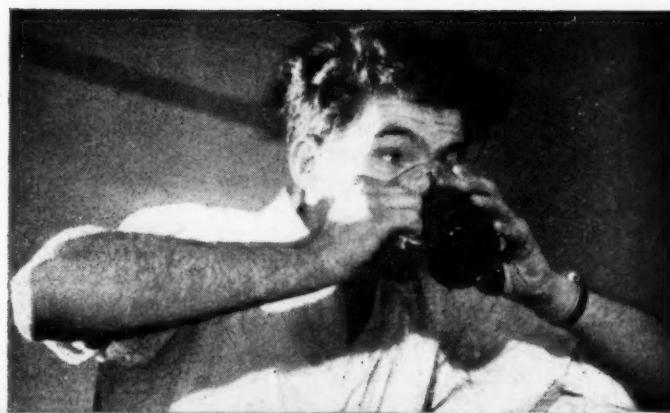
TIMON OF ATHENS IV, III, 152

*Timon.* Consumptions sow  
 In hollow bones of man ; strike their sharp shins,  
 And mar men's spuring. Crack the lawyer's voice,  
 That he may never more false title plead,  
 Nor sound his quilletts shrilly : hoar the flamen,  
 That scolds against the quality of flesh,  
 And not believes himself : down with the nose,  
 Down with it flat ; take the bridge quite away  
 Of him that, this particular to forsee,  
 Smells from the general weal : make curl'd-pate ruffians bald  
 And let the unscarr'd braggots of the war  
 Derive some pain from you : plague all,  
 That your activity may defeat and quell  
 The source of all erection. There's more gold ;  
 Do you damn others, and let this damn you,  
 And ditches grave you all !

*There is no prize for guessing what Shakespeare had in mind !*

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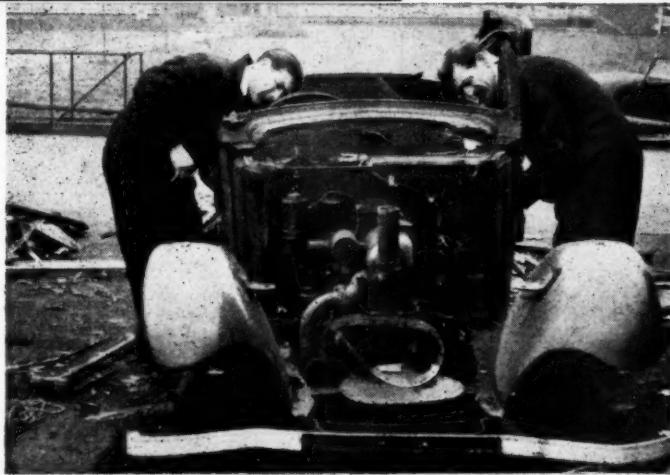
*"Cheers"*



*"Bottoms up"*



*The Medical College  
pursues a strong line  
over derelict cars*



## CALENDAR

## APRIL

Sat. 16—On duty : Dr. E. R. Cullinan  
 Mr. J. P. Hosford  
 Mr. C. Langton Hewer  
 Thur. 21—Abernethian Society : Mr. D. M.  
 Jackson, F.R.C.S.  
 Sat. 23—On duty : Medical and Surgical  
 Units  
 Mr. G. H. Ellis  
 Mon. 25—Film Society : *Strange Incident*  
 Sat. 30—On duty : Dr. R. Bodley Scott  
 Mr. A. H. Hunt  
 Mr. F. T. Evans

## MAY

Sat. 7—On duty : Dr. A. W. Spence  
 Mr. C. Naunton  
 Morgan  
 Mr. R. A. Bowen  
 Wed. 11—VIEW DAY  
 Thur. 12—View Day Ball : Quaglino's Ball  
 Room  
 Sat. 14—On duty : Dr. G. W. Hayward  
 Mr. A. W. Badenoch  
 Mr. R. W. Ballantine

## Deaths

BARFORD.—On February 23rd, Dr. Percy  
 Crompe Barford, aged 91. Qualified 1895.  
 CARTWRIGHT.—On March 2nd, Dr. John  
 Fraser Cartwright. Qualified 1940.  
 DOCKRAY.—On February 21st, Dr. John  
 Dockray. Qualified 1925.  
 GROVES.—On February 25th, Dr. John  
 Nixon Groves, D.S.O. Qualified 1932.  
 LEON.—On March 7th, Dr. Kenneth Leon.  
 Qualified 1922.  
 LONGFORD. On February 10th, Dr. W. U.  
 Desmond Longford. Qualified 1917.  
 McINDOE.—On April 11th, Sir Archibald  
 McIndoe, C.B.E., aged 59.  
 RUSSELL.—On February 7th, Dr. Edmund N.  
 Russell. Qualified 1908.  
 THOMSON.—On February 10th, Dr. David  
 Maitland Thomson, aged 50. Qualified  
 1933.

## ANNOUNCEMENTS

## Engagements

SCORER—JEFFREY.—The engagement is an-  
 nounced between Dr. Michael John  
 Stephen Scorer and Sarah Helen Poppy  
 Jeffrey.

WELLS—TURTON.—The engagement is an-  
 nounced between Dr. David Paulett Wells  
 and Gillian Hermione Christian Turton.

## Marriages

EAST—MERRYFIELD.—On February 12th, Dr.  
 Cecil John East to Eileen Merryfield.  
 GRAY—INSKIP.—On March 5th, Dr. John  
 Maurice Gray to Janet Fiona Inskip.

## Births

DALLAS ROSS.—On February 26th, to  
 Margaret, wife of Dr. W. P. Dallas Ross,  
 a son.  
 DRAKE.—On March 7th, to Doreen, wife of  
 Dr. Patrick Drake, a daughter.  
 DURHAM.—On March 6th, to Mabel and  
 Surg.-Commander Peter Durham, R.N., a  
 daughter (Katharine Eve), a sister for  
 Anthony and Jonathan.  
 FREEMAN.—On February 3rd, to Daphne,  
 wife of Peter Freeman, F.R.C.S., a  
 daughter (Ann Lindsay).  
 HILL.—On February 12th, to Margaret,  
 wife of Dr. John M. Hill, a daughter.  
 LEVIN.—On February 11th, to Alice, wife of  
 Dr. Arthur Levin, a daughter, sister to  
 Richard and Diana.  
 LUMLEY.—On March 3rd, to Fay and Dr.  
 Philip William Lumley, a daughter (Diana  
 Frances).  
 MCKENZIE.—On February 17th, to Sally,  
 wife of Dr. Alexander McKenzie, a second  
 daughter (Tessa Frances Elizabeth), a  
 sister for Miranda.  
 MARKER.—On February 18th, to Helen and  
 Dr. Roy Marker, a son (Ian David).  
 POCOCK.—On February 28th, at the Royal  
 Bucks Hospital, to Angela (*nee* Tresidder),  
 wife of Eric Pocock, M.R.C.V.S., a son  
 (John David William).  
 STRUTHERS.—On March 7th, to Valerie,  
 wife of Dr. John Struthers, a daughter.  
 WHEELER.—On February 5th, to Pat and  
 Dr. Barry Wheeler, a son (David Laurence  
 Reid), brother for Jennie and Guy.

## The Aetiology of Rheumatic Disease

by L. E. GLYNN M.D. (LOND.)

M.R.C. Rheumatism Research Unit, Taplow

The various diseases loosely grouped together as rheumatic, have but two features in common, they interfere with movement, largely, but not entirely as a result of pain, and their aetiology is unknown. It is not surprising that with so little in common the group includes diseases of most diverse clinical features and probably of equally diverse aetiology. Clearly delimited and aetiologically distinct are rheumatic fever with a fundamental causal relationship to the haemolytic streptococcus, rheumatoid arthritis and disseminated lupus erythematosus probably related to some disturbance of immunological tolerance, gout with its undoubted association with uric acid metabolism and osteoarthritis, a degenerative state normal in old age but accelerated by many factors known and unknown. Other well defined conditions whose aetiology is almost entirely obscure are scleroderma and dermatomyositis. Finally, there are several ill defined conditions lacking not only a known aetiology but also largely devoid of known pathology, e.g. fibrositis, neuritis and lumbago.

The aetiological role of streptococci in rheumatic fever was first suggested by Westphal, Wassermann and Malkoff (1899)<sup>1</sup> when they isolated these organisms from the blood of a patient with rheumatic endocarditis. The following year Poynton and Paine<sup>2</sup> published the results of their extensive study of this disease from which they concluded that the causative organism was a special variety or group of closely allied strains of streptococcus viridans. The evidence collected during the next 30 years, however, failed to substantiate these claims, because the vast majority of blood cultures taken during the febrile stage remained sterile and it proved seldom possible to cultivate any organisms from local lesions taken during life. Further, such organisms as were isolated, although usually streptococcus viridans, failed to produce in experimental animals lesions that could be accepted as those of rheumatic fever.

Between 1931 and 1936 Coburn<sup>3</sup> and his colleagues collected strong epidemiological

evidence implicating haemolytic streptococci. They demonstrated, for example, the remarkable frequency with which an infection of the throat by these organisms preceded by 1-5 weeks the clinical onset of rheumatic fever, as well as the frequency with which a relapse followed the recurrence of such a throat infection. These important findings have since been supported by several studies of streptococcal epidemics, notably in army camps in the U.S.A.<sup>4</sup> and in Great Britain<sup>5</sup> during the Second World War.

Further support of the aetiological role of the haemolytic streptococcus came from the study of the level of antibodies to various streptococcal products in the blood of patients with rheumatic fever. The first of these antibodies to receive serious attention was that to streptolysin O and Todd (1932)<sup>6</sup> found a rise in titre of this antibody not only in those cases of rheumatic fever known to have been preceded by a haemolytic streptococcal infection of the throat, but in many patients without such a history. Since the immunological response to different streptococcal antigens may differ widely in any one individual, the evidence for a recent streptococcal infection is enhanced by increasing the number of antigens used. Thus the incidence of a raised antistreptolysin O titre in acute rheumatic fever is about 80 per cent: a similar percentage show a rise in antistreptokinase, but if both tests are used 95 per cent show a rise of one or other, and if four different antigens are used positive results approach 100 per cent.<sup>7</sup>

Confirmation of the aetiological role of haemolytic streptococci in the genesis of rheumatic fever has been obtained in a practical and convincing manner from the successful use of prophylactic measures directed against these organisms in reducing the incidence of clinical recurrences in a susceptible population, i.e. individuals who have already suffered one or more attacks of the disease.<sup>8</sup> The large scale success of such measures in many countries is at present strong evidence for the streptococcal aetiology of rheumatic fever. Failure to find these organisms within the specific lesions and the

characteristic interval between the throat infection and the appearance of rheumatic fever both suggest that the lesions are not caused by the direct local action of the organisms but are the result of a hypersensitivity to one or more of their products. The clear interval thus represents the time required for hypersensitivity to develop. Rich and Gregory<sup>9</sup> have, moreover, claimed that the cardiac lesions in rabbits that develop as a result of repeated massive injections of foreign serum are virtually identical to those of rheumatic fever. Against this simple hypothesis however must be set the following observations:—Despite the close similarity of the lesions produced by Rich and Gregory to those of rheumatic fever they are nevertheless distinguishable from them. No one has succeeded in producing experimental lesions identical to those of rheumatic fever by injecting streptococcal fractions or products. Although tests in human cases of rheumatic fever for hypersensitivity to various streptococcal products give more positive reactions than normal subjects, many of the test subjects are negative and many controls positive.<sup>10</sup> Finally, it is difficult on this hypothesis to explain why the undoubtedly relationship of the disease to streptococcal infection does not extend to related micro-organisms.

In recent years there has been a growing realisation that some diseases may be caused by a breakdown in the immunological tolerance of an individual to one or more of his own antigens, and rheumatic fever is one of the diseases which might arise in this manner. Of the various ways in which a breakdown of immunological tolerance can be achieved the alteration of a body protein by interaction with a foreign antigen is the one most readily brought about. This, for example, underlies the development of thrombocytopenic purpura in some individuals as a result of taking Sedormid. As Ackroyd<sup>11</sup> convincingly showed, the platelet-sedormid complex acts as a foreign antigen to which specific antibodies are formed. The subsequent interaction between this antibody and the platelet-sedormid complex results in clumping and elimination of the platelets. It will be noted that in this situation a complete antigen capable of eliciting an auto-antibody response has arisen by the complexing of an exogenous hapten, Sedormid, with an endogenous protein, the platelet. It is conceivable that an antigen similarly

capable of exciting an auto-antibody response could arise from the interaction of an endogenous hapten, e.g. a polysaccharide, and an exogenous protein, e.g. a streptococcus. That haemolytic streptococci are capable of adsorbing minute amounts of non antigenic polysaccharides and converting them to complete antigens has now been demonstrated with a number of vegetable polysaccharides<sup>12</sup> as well as with several human blood group substances.<sup>13</sup> We have therefore suggested that the role of the streptococcus in the pathogenesis of rheumatic fever may perhaps be a similar conversion of some tissue hapten to complete antigenicity, the lesions resulting from the subsequent interaction of such an antibody with the hapten wherever in the body the latter is to be found.

It must be admitted, however, that there are several weak links in this hypothesis, the most important of which is the failure so far to induce a true auto-antibody as distinct from an iso-antibody by this technique. Of perhaps equal significance is the absence from the plasma of patients with rheumatic fever of any demonstrable antibody against any known tissue antigen. Recently, however, Kaplan<sup>14</sup> has found such an antibody that specifically reacts with an antigen in the subsarcolemmal cytoplasm of cardiac muscle.

A notable feature of the relationship of haemolytic streptococcal infections to rheumatic fever which any satisfactory hypothesis must account for is the small proportion of individuals suffering such a throat infection that subsequently develops rheumatic fever. The data from several epidemics in widely different parts of the world indicate that this occurs in only about 3 per cent of such infections.<sup>4</sup> Yet another significant factor is the virtual absence of rheumatic fever following streptococcal infections elsewhere in the body, e.g. erysipelas or puerperal sepsis. This strongly suggests that not only is there something peculiar about the throat environment, but also that there may well be certain features in the throat peculiar to those capable of developing rheumatic fever. A well known variable simple to investigate is the presence or absence in the saliva of an individual of his ABO blood group substance. Such a study of 611 patients with rheumatic fever showed that the incidence of non secretors was significantly higher than in a control group of 1,129 normal schoolchildren.<sup>15</sup> The hypothesis put forward to

explain these figures suggests that only those individuals homozygous or heterozygous for the non-secretor gene are capable of developing rheumatic fever; individuals homozygous for the secretor gene can not, on this hypothesis, develop the disease. Whether this be true or false the significant difference established between the two groups emphasises the importance of the throat environment in determining whether or not a streptococcal infection of the throat is to be followed by an attack of rheumatic fever.

In none of the other diseases of the rheumatic group is an aetiological agent so clearly implicated as is the haemolytic streptococcus in rheumatic fever. In both rheumatoid arthritis (R.A.) and disseminated lupus erythematosus (D.L.E.) however, the accumulating evidence of recent years points strongly to the participation of some disturbance of the individual's immune mechanism. Since the early days of immunology the ability of an individual to distinguish its own antigens from those that are antigenically foreign has proved an intriguing phenomenon and for many years it was regarded as impossible for an animal to produce an antibody response to such an auto-antigen. Several factors, however, have combined to weaken resistance to the concept of auto-immunity, i.e. immune reactions directed against an individual's own antigens. The demonstration that acquired haemolytic anaemia is frequently associated with the presence of antibodies specific for one or more antigens on the red cells emphasised the need for a reappraisal of the problem. The experimental production of a variety of lesions, e.g. encephalitis,<sup>16</sup> thyroiditis,<sup>17</sup> adrenalitis<sup>18</sup> and azoospermia,<sup>19</sup> by the parenteral injection of organ emulsions with an adjuvant such as Freund's that is known to enhance immune responses provided further evidence implicating auto-immune mechanisms in pathogenesis. Furthermore, the nature of the lesions obtained in these experiments bears such close resemblance in many instances to those of some human diseases of unknown cause that the role of "auto-immunity" in pathogenesis is rapidly commanding wide acceptance. An equally important contribution to this change in mental attitude is our increased understanding, thanks to the work of Medawar and his colleagues,<sup>20</sup> of the mechanism of immunological tolerance. They have shown that the ability to recognise an antigen as foreign is largely determined by

the absence of that particular antigen when the antibody-forming tissue is coming to maturity, i.e. at about the time of birth. In consequence, if a foreign antigen be introduced into an individual at about this time, the ability of the individual to respond immunologically to a later exhibition of the antigen will be lost or significantly impaired. They were able to show, for example, that a mouse can be induced to accept a skin homograft if the recipient receives at about the time of birth a parenteral injection of cells from the prospective donor. It is apparent from these and similar experiments that in a normal subject a recognition mechanism exists enabling the antibody-forming tissues to differentiate self from non self. How precisely this differentiation is achieved is the subject of much speculation and experiment. The important fact, however, is that such a mechanism exists: and like all other known mechanisms must be subject occasionally to defect or breakdown. The problem today is to what extent are any of the rheumatic diseases the result of such a defect or breakdown?

In both R.A. and D.L.E. phenomena have been described which are indeed most readily explained as examples of auto-immune reactions. The presence in the great majority of rheumatoid arthritics of a serum factor capable of agglutinating sensitised erythrocytes<sup>21</sup> has been shown to be due to the presence of a  $\gamma$ -globulin, the so called rheumatoid factor, with a specific affinity for aggregated or slightly altered  $\gamma$ -globulin of widely diverse animal, including human, origins. This rheumatoid factor is itself a component of the  $\gamma$ -globulin fraction with a sedimentation coefficient of 19S to which many known antibodies belong. It is apparently synthesised like other antibodies by the plasma cells and its reaction with aggregated  $\gamma$ -globulins has most of the features of an antigen-antibody reaction. There is, however, no evidence that this factor is in any way responsible for any of the lesions of rheumatoid disease.

In the same way, the factor in patients with D.L.E. that is responsible for the positive L.E. cell test, so characteristic of this disease, is apparently one of a group of antibodies directed specifically against various components of cell nuclei, such as nucleoprotein or histone.<sup>22</sup> Here, too, as with the rheumatoid factor, no pathogenic role can be assigned to these antinuclear factors.

in the evolution of D.L.E. This raises the important question of the role of circulating antibody in the pathogenesis of any autoimmune disease, a question that has been especially emphasised by the high incidence of rheumatoid arthritis in patients suffering from congenital agammaglobulinaemia. It must be recalled, however, that many immunological phenomena are known which are apparently independent of circulating antibody. Outstanding amongst these is the tuberculin reaction which is presumably mediated by the specific sensitisation of leucocytes (probably lymphocytes) since it can be readily transferred passively by such cells, but not by serum. Presumably, if R.A. and D.L.E. are indeed examples of autoimmune disease, the immunological reaction is of this delayed type and the specific serum factors are to be regarded as but bye products of the more fundamental immune reactions of the cells.

Even if it be accepted that these diseases are the result of auto-immune reactions there is at present little evidence to indicate how or why the breakdown in tolerance has occurred. Useful clues may perhaps be obtained from the study of other diseases more definitely mediated by auto-immune mechanisms, such as Hashimotos thyroiditis<sup>24</sup>.

Here it has been suggested that tolerance has never been acquired as the antigens concerned are normally confined to the gland with little chance of access to the antibody-forming tissues. But many other theoretical possibilities exist and no doubt the manner of tolerance breakdown may well vary from one disease to another. One important possibility recently advocated by Burnet<sup>24</sup> attributes the loss of tolerance to somatic mutation of antibody-forming cells with the emergence of a clone of cells that has lost the tolerance acquired during the critical neonatal periods. Since somatic mutation is presumably a constantly occurring process, it is necessary to postulate that normally there exists a homeostatic mechanism for the suppression of such non-tolerant clones. Breakdown of tolerance thus becomes breakdown of this homeostatic mechanism: but whether this brings one any nearer to a solution of the problem of immune tolerance may well be questioned. Nevertheless, despite the present inability to understand the complexities of immune tolerance, and although auto-immunity as a pathogenic mechanism is still open to question, these concepts at present have no equals as stimuli to research in the field of rheumatic disease.

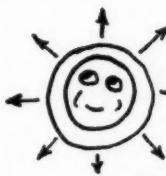
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## PFEIFFERELLA



TIME WAS I WAS  
NICE, HARDWORKING  
AND ORTHODOX



I WORKED ALL DAY  
MAKING LYSINES-  
OPSONINS-  
AGGLUTININS- ALL  
KINDS OF ANTIBODIES



COMPLEMENT  
FLOWED IN  
ALL DAY LONG



I LIKED  
MY WORK



THEN THEY  
STARTED  
ANTIBIOTICS



I WAS  
REDUNDANT



THEN I HEARD  
ABOUT  
AUTO IMMUNE  
DISEASE



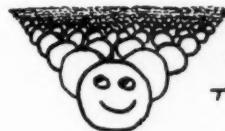
"WHAT YOU NEED  
IS A FORBIDDEN  
CLONE"



IT DID SOUND BOLSHEE  
BUT — LOOK I WAS  
DESPERATE



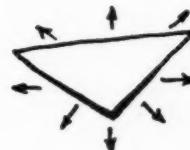
SO I WENT FOR  
A BRAINSHASH  
AND A SOMATIC  
MUTATION



AND SOON I WAS  
THE FATHER OF  
THE CUTEST CLONE



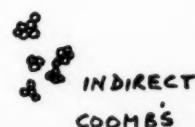
THEN WE HAD AN  
ENCOUNTER  
WITH A LUSCIOUS  
SELF ANTIGEN



AND WE ALL  
MADE ANTIBODY



AND WHEN SHE  
CAME BACK  
SHE HAD A  
POSITIVE —



THEY WON'T CURE  
THAT WITH  
12 MILLION UNITS  
OF PENICILLIN!  
J.M.

## Treatment in Rheumatic Diseases

by H. WYKEHAM BALME, M.A., M.D.(CANTAB.)

St. Bartholomew's Hospital

Patients suffering from rheumatic diseases can nearly always be improved, often very greatly. The principles of treatment that must be followed are quite simple.

### *Inflamed Joints*

It is well known that inflamed parts must be kept at rest, but it seems to be by no means well enough known that inflamed joints will be improved by rest also. Obvious enough in acute gout or in suppurative arthritis, where the slightest movement causes severe pain, the effect of rest is far too often overlooked in the milder joint inflammations and exercise wrongly prescribed instead. In the case of rheumatoid arthritis the patient himself commonly influences his doctor in this direction, having found that exercise helps him to work off his morning stiffness; but this is an entirely different matter, and it is quite definite now that just as rest leads to subsidence in the activity of a tuberculous joint, so it also leads to a lessening of the inflammation in a rheumatoid joint.

The methods of resting joints are now well established, thanks to the ingenuity of the orthopaedic surgeons. Plaster of Paris is the main standby, and calcium sulphate, applied externally, thus becomes our most important prescription. In this context its function is purely protective, the splint keeping the joint quiet and in the proper position. It may be necessary only to wear it at night, but it is often feasible, and a good thing, to provide splints for use in the daytime too, the patient wearing them then and even working in them. If a joint is expected to give trouble for a long time materials other than plaster of paris may be used, such as plastic or Glassona—and these have the advantage of being washable and more durable—but in any case it is always better to tailor-make the splint rather than to use ready-to-wear metal or wooden ones.

The wrists, which are so often affected in rheumatoid arthritis, can be beautifully protected in this way. When the knees are affected splints can be made to be worn only at night, and after the first few uncomfortable nights have been spent in these the patient

will soon start admitting that his knees are better. It may even be worth while encasing one knee in a complete cast for a week or two and allowing the patient up and about in it. The feet are very difficult to splint, but here the surgical shoe maker comes to one's assistance, and his work is of vital importance. A stiff deformed foot is very painful and crippling so it is essential, directly trouble starts there, to provide proper shoes which fit well and support the foot all round. It is a good working rule to provide them as a matter of urgency if the patient finds that he gets about better in slippers than in his ordinary shoes. The neck, which is often affected, can be immobilised by a collar, of which various designs are now available.

### *Ill Patients*

Patients who are ill will become less ill if they rest in bed; arthritic patients may be made quite ill by their disease, and in these cases rest in bed is beneficial too. This applies not only to acute conditions such as rheumatic fever and serum sickness but also again to rheumatoid arthritis, and a surprising thing is that following a period of only a few weeks of proper rest the joint condition may continue to improve even after the patient is up and about again.

### *Damaged Joints*

Normal joints are kept healthy by being used, and prolonged disuse of a normal joint is unkind to it. Joints that have been damaged, but are not inflamed, can be greatly harmed by prolonged disuse, capsular adhesions forming readily and limiting movement severely. On the other hand, excessive use of a damaged joint will lead to traumatic inflammation in it and will cause further damage; and in the same way weight-bearing, which is good for a normal joint, can be very harmful indeed to a damaged one. One has to be careful therefore in estimating the extent to which a damaged joint can safely be used.

Severely damaged joints may be able to tolerate very little movement or weight-bearing, and if there is much pain arthrodesis,

or perhaps arthroplasty, often offers an excellent solution. Less damaged joints can often be kept comfortable if unnecessary strains are avoided, and by this means further damage may to some extent be prevented. The stability of the knees for instance is dependent on the strength of the quadriceps muscle, so if they are damaged exercises to keep up the strength of the muscle help a great deal. In the case of osteoarthritis of any weight-bearing joint obesity is obviously very harmful, and it is often necessary to insist that such patients lose as much as half a hundredweight.

After they have achieved this it may be possible to increase the mobility of the joint, and eventually lessen the pain in it, by persevering with active exercises. Exercises will also help to improve the mobility of a joint damaged by previous inflammatory disease, but it is obviously important to make sure that they are not excessive enough to cause a recrudescence of inflammation. The exercises will inevitably be uncomfortable or even painful, so it is a good idea to make the joint more comfortable first by applying heat and perhaps some nice consolatory massage. Mobilising a joint that has become stiff in a bad position can be a very difficult task and sometimes impossible. The problem arises very frequently indeed, particularly in the case of the knees and wrists which too often become fixed in flexion, even (bow your heads in shame !) when the patient has throughout his illness been under medical care. Serial plasters, perhaps with manipulation (by an expert only !), often do the trick, but osteotomy may be necessary.

#### *Cripples*

Patients who are not ill will be made fitter by exercise ; arthritic patients who are not ill will be benefitted by it too. Sometimes exercise becomes of overriding importance, even in spite of the persistence of mild joint inflammation, and an outstanding example of this situation is provided by ankylosing spondylitis. In this condition the patients are not usually ill, despite their high E.S.R.'s—as ever a rotten guide—and the more they are rested the more their joints will ankylose. They must be exercised skilfully and unmercifully.

A very stiff upper lip is required of arthritic cripples when the time has come for them to get on their feet again. Self-pity at this stage is fatal, and if they have been neglected for long and have the inevitable joint con-

tractions and muscle wasting as a result, much determination will be required of them. Following orthopaedic correction of those deformities that require it, the basic principle of rehabilitation consists in exercise. Special efforts are made towards restoring those movements which are particularly necessary for the patient's independence, such as feeding himself. Even after maximal improvement has eventually been obtained, it is still possible to help the patient immensely by providing him with gadgets, such as thick-handled knives and forks, levers on water taps, a heightened seat on the lavatory, a long handle to his razor, and a rail to grip on so that he can get out of his bath. If plenty of ingenuity is used even the wheelchair life that the severe cripple may be forced to lead can be rendered quite endurable and come to allow of a little independence.

#### *Special Considerations*

**Pain** : Analgesics are not the whole answer to pain in rheumatic conditions. Immobilisation for inflammation and mobilisation for mere stiffness are the first steps. Keeping the part warm with suitable clothing and soothing it down with the actual application of heat are the second. Bracketed with this is the use of counter-irritation, which is still as strangely effective now as ever it was : old-fashioned Scott's Dressing, buttered on lint and applied to an osteoarthritic knee, is certainly worth remembering. Next in importance comes aspirin, which is very effective so long as the pain is not severe. The patient is usually frightened to take enough of it and may have to be persuaded to do so, but the relatively mild pain of rheumatoid arthritis will usually be controlled if he will take 60 to 100 grains (12 to 20 tablets) of it daily. The severe pain of gout or of a bad osteoarthritic hip will not really be touched by it, however. Ordinary cheap aspirin should usually be prescribed, as there is disappointingly little advantage in the fancy soluble varieties.

Stronger than aspirin is phenylbutazone ("Butazolidin"), and as long as its dose is kept to 400 mgm. a day or less the risk of toxic effects is reasonably small. But it is not usually necessary to prescribe it. For the pain and stiffness of ankylosing spondylitis however, it seems to be remarkably effective and may be used preferentially. Steroids are not analgesics and are not to be used as such.

**Insomnia** : Do not go messing about giving barbiturates to patients who are kept

awake by pain. Splint the painful joint so that it will not be inadvertently moved in bed, give plenty of aspirin, and your sleep-starved patient will require no hypnotics from you.

*Anxiety* : This, rather than pain, may well be the cause of insomnia, the patient, reasonably enough, worrying during the night hours over the prospect of crippledom. Barbiturates will in no way dim this nightmare but will rather, by causing mental confusion, render it more vivid. A doctor's optimism and cheerful competence are what is required here, not a putting of the head in the sand, and it is astonishing to see how morale improves when the patient realises he has at last found a doctor interested in his condition.

*Gout* : Acute gout responds miraculously, and entirely mysteriously, to colchicine, 1 mgm. every 2 hours by mouth until the pain abates or until diarrhoea or the threat of it arises. Usually about 6 doses are needed; thereafter 1 mgm. t.d.s. for a few weeks until the attack is over. If the patient is intolerant of it, phenylbutazone, in biggish doses (600 mgm. to 1.0 gram daily for a few days), can be used. Steroids are almost never required.

Chronic gout responds well to uricosuric agents, acute attacks lessening in number and severity and tophi disappearing; probenecid ("Benemid") 1.0 to 2.0 grams per day is nearly always effective, but newer and more potent drugs are on the way. Salicylates are not good uricosuric agents and are not advised; moreover they inhibit the action of probenecid and must not be used in conjunction with it. Cinchophen used to be used, but killed a few gouty victims off by destroying their livers and is now obsolete. With colchicine and probenecid little else is required in the treatment of gout, and no great dietary restrictions need usually be imposed on the ordinary abstemious Englishman. A good fluid intake will protect against uric acid calculi (which are rare); perhaps it might be wise to recommend that the fluid used should be bland.

*Radiotherapy* : There is some, but not much, doubt that radiotherapy temporarily lessens pain and stiffness in active ankylosing spondylitis. There is more doubt whether it halts the disease or even slows its progress. There is much doubt whether it in any way acts as a prophylactic or ought to be used early. There is no doubt that it increases the risk of leukaemia (though I doubt

whether the riskiness of it is any greater than the riskiness of the M.I.). And it certainly can only be used sparingly at any one site or the skin will give way.

*Gold* : If it works at all, gold works best in those cases of recent acute or acute-ish rheumatoid arthritis in whom the prognosis is in any case good. Advocates claim that it works best if it nearly kills the patient first. It is very difficult to tell if it has any effect that is worth while when set against this toxicity: two thirds of rheumatoid sufferers will improve anyway; even more of those for whom it is considered indicated will improve anyway; and the outcome in any given case if left untreated is always impossible to tell.

*Chloroquin* : This again is said to work best in acute or acute-ish rheumatoid arthritis; but even the makers do not claim that it has any effect in under a month or more, by which time many cases would have spontaneously improved immensely. It works in discoid lupus erythematosus; it appears to work in disseminated lupus erythematosus; it probably helps a little in some rheumatoids. But it is reasonably non-toxic and can happily be given if you like.

*Steroids* : Steroids can achieve miraculous improvement in some cases of rheumatoid arthritis if they are used properly; but there are some things they cannot do and some terrible things they can do. They are no substitute for rest, and if either the patient or his joints require rest they must have that first. They are in no sense analgesics, and the mere severity of pain is of no relevance as an indication for their use. They have risks to life and obviously should not be used in mild cases; and if spontaneous remission seems likely it is surely sensible to wait and see if it will occur. To give them just for good measure for a short time and then stop them, or in general to fiddle about with their dosage, not only achieves nothing in the way of benefit but in effect gives the patient a medical adrenalectomy and is downright wickedness.

Among the rheumatic diseases rheumatoid arthritis is their main indication, but even so less than 5 per cent of those rheumatoid sufferers bad enough to attend hospital require treatment with them. Their effect is to reduce the intensity of the inflammation—in the joints, synovial sheaths, tendons, bursae, subcutaneous nodules—and at the

same time to make the patient feel better. But unfortunately if they are used alone, and not in combination with other forms of treatment the most important of which is rest, they are very rarely adequate. It is true that in a very small proportion of cases the patient is restored virtually to normal with quite small doses of steroids well within the limits of immediate safety. The much greater majority, however, would require doses outside the limits of safety, and the dangers of this get steadily higher as the months go by. Worse still, a sizeable proportion of these patients would require their already high steroid dosage to be still further increased as time goes by if they are to remain free of symptoms. The end result is that the patient is rendered dangerously ill with the excessive dosage, and becomes severely demoralised, with his arthritis remaining uncontrolled in spite of everything.

Steroids are to be used as a strategic and not as a tactical weapon. The most they are likely to achieve in safety is a moderate lessening of the severity of the disease, and if used alone this effect is far from dramatic. If a patient with bad rheumatoid arthritis however is first rested, both himself if need be, and certainly his joints, then the steroids can really make an immense difference. If the rest and the analgesics are persevered with alone for a few weeks it may be found that quite small doses of steroids are all that is required to get the patient reasonably mobile and to keep him thus more or less indefinitely. Usually he will have to accept the position that the relief allowed him is only partial, so it is wise to start low and not with an initial high loading dose. This also means that he must still be watched over in case individual joints start needing local treatment again, arising out of the continued activity of disease. This combination, rest plus steroids, is the sort of regime that is suitable for a fair number of the real rheumatoids—those with nodules, toxicity, anaemia, weight loss, bone destruction and generalised illness, and not merely a few swollen joints—and evidence is now accumulating that not only does it make them better for the time being, but that it actually slows down the disease and improves the ultimate prognosis.

Steroids can also be injected into joints, and exert a local action there; but from what has already been said, this will not often be necessary. Inevitably there is some risk of infection, particularly as the injections

usually have to be repeated every few weeks for a long time. But if persistent activity in one joint is particularly disabling this can prove a very useful trick. Naturally, steroids can do nothing to improve a destroyed or disorganised joint, whether applied locally or given systematically; in the absence of the signs of inflammation there is no point in using them.

The most widely used steroids just now are prednisone and prednisolone. They have definite advantages over cortisone, which in this connection is obsolete. Ten mgm. of either a day is about the highest safe maintenance dose, and one prefers it to be less; over 15 mgm. daily is definitely dangerous and not justifiable in these non-dangerous diseases. Of the newer steroids, methyl prednisolone seems to have no advantages over prednisolone; triamcinolone causes queer side effects including sometimes much loss of appetite and has not proved satisfactory; dexamethasone on the other hand may cause such uncontrollable greed that the patient may quickly gain two or three stone, and I have known one put on 13 pounds in one weekend of glorious eating. This is not kind to weight-bearing joints. Alternatively one can use ACTH by subcutaneous injection, and this method has its advantages, but although the material is more uniform and reliable nowadays than it used to be the patient's response to it remains variable, and for long-term use this means that some measure of the adrenal stimulation must be regularly applied. The usual thing is to measure the urinary output of 17-hydroxy-corticosteroids, an aliquot of the measured 24 hour sample being sent for analysis weekly. For local action one uses hydrocortisone or its analogue prednisolone, as much being put into a joint as one comfortably can—say 50 mgm. for a knee, 5 mgm. for an acromio-clavicular joint.

*Focal Sepsis*: A septic lesion anywhere is a pretty nasty thing to have, and it may make one mildly ill; if one is already ill with a chronic disease it is even nastier to have, and it may be even more effective in making one more ill. Nowadays one does not search for focal sepsis in rheumatoid arthritis, theories of etiology having changed, but if one sees it one deals with it so that the patient will feel better.

#### *In Conclusion*

Incurable diseases are not necessarily untreatable; on the contrary, a disease that is

incurable requires more treatment than one that is curable. This is really very obvious. The exciting thing about the rheumatic diseases is that with care, and attention to detail, quite astonishing results can be obtained and they prove to be eminently treatable although neither cause nor cure is known. The secret lies in the careful assessment of each patient: deciding to what extent pain is due to inflammation, to mechanical stress, or to fear; distinguishing between reversible and irreversible joint damage; estimating how ill the patient is and how much in need of rest, whether he has the moral courage to work with you in the long and painful months ahead, or how much he is addicted to invalidism and will resist your efforts to improve him; making

some reasonable prognostic guess as to whether the disease will remit, or whether it will inexorably progress and justify you in the taking of therapeutic risks.

The subject brings one into close relationship with orthopaedic surgeons and with physiotherapists (the latter not the least of its compensations) and is often mistakenly identified with physical medicine, but I would earnestly advise that nobody take it up as an exclusive speciality unless he has first for some years been properly immersed in general medicine. For these are general medical diseases and not just disorders of joints. It is the patient as a whole that is in need of treatment, and to treat him properly it is necessary that one be thoroughly used to dealing with whole patients.

## The Social Problems of Rheumatic Disease

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The social problems of rheumatic disease are many and varied, depending largely upon the diagnosis. Those suffering from rheumatoid arthritis with either severe crippling or the fear of it, are likely to be faced with the most problems, although osteo-arthritis and those suffering from non-arthritis forms of rheumatism may also have theirs.

In cases of rheumatoid arthritis the prolonged nature of the illness and the variable prognosis create serious problems, to which, very often, no end can be seen. No hard and fast social plan can be made, and the patient's personality and attitude to their illness become vital. The patient not only has to learn to live with the disabilities he has at the present moment, but he may have to adapt himself at longer or shorter intervals to increased disabilities, with the uncertain hope that his arthritis will eventually burn itself out. Problems of this sort often are in connection with the patient's job. Mr. W., a man of 45, was a bricklayer, and had arthritis for a few years. His condition was deteriorating and he began to worry about the future. He was naturally reluctant

to face a change of job, as he knew this would almost certainly mean a drop in pay, and he had fairly heavy financial commitments. After a short spell off work, and with winter weather looming closer, he was prepared to consider a change. He was registered as disabled at the Labour Exchange, and as he fortunately lived in an area where there was a training centre, the Disablement Resettlement Officer was able to arrange for him to train as a typewriter mechanic. On completing his training he got a job near his home. All through this period he had been having treatment for his arthritis. After eighteen months in his new job his condition flared up, and he was advised to have in-patient treatment, and then to have an operation on his elbow. While in hospital he was extremely worried and depressed about employment prospects and his ability to use his tools again, particularly as his old firm had closed down. He needed constant encouragement, as he thought that his retraining might have been all in vain. However, he was determined not to depend on his wife's earnings, and after applying for

various unsuitable jobs, found one near his home as a typewriter mechanic. Without determination to help himself he might well have drifted along either unable to work, or in some unproductive and frustrating "light" job.

The patient may appear to have some simple problem, such as the young housewife who needs a home help to relieve her of some heavy chores and thereby avoid stress and strain. This may, however, mask the real social problem of the patient's attitude to her arthritis. Mrs. J., a woman of 34, is married to a schoolmaster and has two children under school age. She has had rheumatoid arthritis for about ten years, and had a flare-up after the birth of the second child. She is anxious to keep her home nicely and give her children all the care and affection she should. She was becoming increasingly tired and, as her general health deteriorated, her arthritis also got worse. She realised that she must have help to break the vicious circle, but thought the family could not afford a home help. The acceptance of chronic disease and the replanning of her daily routine and of the financial pattern of expenditure was the real problem which faced her. Fortunately she was intelligent and had an understanding husband, so that she was enabled to do this. Inevitably she still has periods of overwork, e.g. when the children are ill, but she has learnt how to meet her difficulties and does not feel so inadequate when she accepts help, or makes plans for the children so that she can rest.

The endless nature of the rheumatoids' problems is illustrated by the case of Mrs. M., a widow of 58. She has had rheumatoid arthritis for many years and has struggled to bring up her family of three children, who are now married, and she lives alone. She is immensely independent, hates asking for any help, even from her daughter and son-in-law who live upstairs, and prefers to do everything for herself in spite of grossly disabled hands and very painful knees and other joints. A typical pattern of ups and downs emerges—she is sent to a Spa for a month in the summer, and with treatment, good meals, rest and no worries, comes back feeling fine, and able to cope with her pains and family worries. Gradually during the winter, her health deteriorates a little, she loses her appetite, she has more to do when her daughter has 'flu, her arthritis gets more painful, she worries more about her family,

she feels an unwanted burden, her pain gets worse, she can hardly face the journey to a Spa when it is suggested, but is encouraged to go and is physically and mentally built up for another year. The problem is to enable this patient to have all the help that is available from community sources without undermining her independent spirit, and to give her encouragement over the bad patches.

Both mental and physical strain are social factors affecting the rheumatoid arthritics, and in many cases nothing can be done to ease the situation. For example, the young married woman living with in-laws, may be fond of her relatives but feels unhappy and frustrated that she cannot run a home of her own as she likes. An elderly woman may have a landlady who is entirely unsympathetic and who seems to make difficulties for her arthritic tenant. The man, who is the breadwinner of the family, has the constant fear that he may be unable to earn, and will stay in a dull and frustrating job rather than risk a change to one where he might be happier.

Many arthritics live in most unsuitable "flats," particularly in some older London houses where water often has to be carried up and down two or three flights of stairs, and the only lavatory may be in the yard at the back. Even if the flat is all on one level the occupant may be virtually marooned owing to his or her inability to negotiate stairs. If someone living alone is thus prevented from going out, he or she often will find it very difficult to accept the fact of their dependence on others, whether visiting friends and relatives, or welfare services such as Home Help, District Nurses, Meals-on-Wheels, etc. A problem which comes to the older rheumatoid arthritics living alone is how long can they continue in their own homes. Miss C., aged 60, could hardly move across her room, but she was determined not to go into a home if possible. She had always been the slave of her family, and when her parents died, she was at last able to live an independent life. She fought hard to maintain this independence and although her own general practitioner, her relatives, the consultant, almoner and physiotherapist at the clinic where she had treatment, all thought she was quite unfit to live alone, she struggled on for some years until she finally was entirely dependent on a neighbour helping her to move at all. She then agreed that she must

go into a home where she could have nursing care.

Many of the same social problems arise with osteo-arthritis, but generally not in such an acute form because there is not the fear of serious incapacity and crippling, even at an early age, as there is in rheumatoid arthritis. If one joint is affected, and the patient realises that he or she must avoid wear and tear on that joint, the patient can often adjust his or her life without any serious social problem arising. Many people, however, are reluctant to face the evidence of advancing years, and to admit that they must do less. For example, the house-proud woman, who has always kept her house spotless, done all her own laundry, and looked after the garden, and suffers from osteo-arthritis of the knee or hands, even though she admits her joints are worse after a heavy day's work or spring-cleaning, cannot accept the idea of having help or using a laundry.

Some of the problems have a different emphasis, when they affect the older age group. A man of 60 or so with osteo-arthritis of the hip, who has been in a job involving much walking, may well find employers reluctant to take him on for a sedentary job, even if he has the inclination and knowledge. However, by the time he has reached that age, he may not be quite so concerned at the thought of a reduced income, as his family will probably have left school and be more or less independent. He may therefore be readier to take any job that is offered even if it is less lucrative.

Even if severe crippling may not be expected with the resulting social problems, a rheumatic condition may be aggravated by tension, stress or strain. A woman in her 50's may only have minimal osteo-arthritis in her spine, but this can be grossly aggravated by her social situation. She will have a job

to hold down, with the possible fear that she may be supplanted by someone younger. She may have one or both elderly and infirm parents to look after, and this may mean that all her spare time from her job is devoted to household chores and shopping with little or no time for rest and relaxation, possibly not even a proper holiday each year. Even if she has domestic help, she will have the responsibility of running the home and keeping her parents well and contented. If she takes time for treatment of any sort, this increases the pressure either at her job or at home. If she can be helped to see the effects of stress and strain, she may be able and prepared to help herself by having a proper holiday and getting her parents cared for temporarily.

Many practical suggestions can be made to help the rheumatic sufferers to overcome individual difficulties and obtain independence. A long-handled shoe horn, elastic shoe laces, and a stocking aide may make a woman with stiff hips or knees entirely independent in dressing. A long pick-up stick, a raised chair and lavatory seat, may mean that a severely disabled arthritic can be left happily alone at home all day. A razor with a long handle will enable a man with limited use of hands, arms and shoulders to shave himself and not depend on his wife's help to get off to the office in the mornings.

Even with all the available resources for advice and practical help in dealing with social problems, some patients do not seem to have the courage and personality to cope with them. Many arthritics who are severely disabled, make light of the disabilities and do jobs which may appear impossible for them. In the same way, some accept and make the best of difficult and often insoluble social problems, while many others can be helped to do so.

## Research at Bart's

### DEPARTMENT OF MEDICAL STATISTICS

The Department of Medical Statistics is probably the newest as well as the smallest of the separate departments whose work is being described in this series of articles. But although the department is barely more than ten years old, its roots go back to the middle of the nineteenth century. In 1859 the first registrar to the hospital was appointed—a physician whose task was to supervise the "registers" and to compile from them the annual Statistical Tables. However, in the course of time, other duties pressed in on the registrars (a second was appointed in 1864) and the last volume of Statistical Tables that they produced was in 1932.

After the war the present department was set up with the primary task of compiling the annual Statistical Reports. These include tables giving details of the diagnoses of inpatients, surgical operations performed, etc. ; whilst they may provide material for research, they cannot themselves be classed as research and therefore do not come into the scope of this article.

#### *Are these figures significant ?*

To many research workers the essence of statistics may be summed up by the question : "Are these figures significant ?" Before describing some of the work actually carried out in the department, it may be useful to describe the contribution of statistical ideas to medical research in terms of this question. What the questioner usually means is "Do these figures prove what I want them to prove ?" To take an imaginary example : a doctor has treated 30 patients suffering from a particular disease with a new drug and found that 60 per cent have recovered compared with 40 per cent on the standard treatment. Does this prove that the new drug is better than the standard treatment ? From a purely commonsense standpoint the answer is obvious : "It depends." It depends on whether the two groups of patients were comparable, whether the criteria of recovery were the same in each group, whether the patients or the doctor were biased in any way. Only after assuring oneself on these and many similar points, or, to use the current phrase, that the trial has been "properly controlled," is it relevant to ask the question about significance ; "Is

there a statistically significant difference between the two cure-rates ?" or "could the observed difference between the cure-rates have occurred by chance ?" These questions can be answered in precise terms by means of a simple mathematical formula (the chi-squared test).

The point of the foregoing example is to show that the purely mathematical aspect is the last, and often the simplest, problem in assessing the results of a therapeutic experiment. The science of statistics is as much concerned with the design of experiments as with their analysis.

#### *The Sequential trial*

A type of investigation which has recently become popular is that known as a sequential trial. In the standard clinical trial, of the type which has been widely used by the M.R.C. during the last fifteen years or so, it is necessary to determine the size of the trial in advance. Even if the early results appear to show overwhelming preference for one of the two treatments, one is not, strictly speaking, permitted to draw conclusions until the trial is finished. Such a procedure may be wasteful of time and energy and, what is worse, ethically indefensible. The sequential method of comparison is, in effect, a statistical trick which enables the significance of the results to be assessed as they become available.

The principles underlying the method may be illustrated by a trial now being carried out by Dr. M. A. Smith, of the Skin Department, and designed to compare the efficacy of a new anti-pruritic drug with that of a placebo. Each patient is treated for a week with the drug and a week with the placebo ; at the end of a fortnight he is asked which he prefers.

There are two points to notice in the design of the trial ; both arise from the fact that almost the only useful criterion of the effect of the treatment of pruritus is the patient's own, often highly subjective, judgment. It will therefore be difficult to make a valid comparison unless the patient acts as his own control ; fortunately we were able to arrange this as the drug is a short-acting one and the condition relatively chronic. But the more important point is that every possible precaution must be taken

to avoid bias ; the patient must have no clue as to which is the active drug ; he might easily, for instance, think an unusual-looking pill more potent than one that looked like an aspirin (fortunately most drug firms are now often prepared to provide dummy pills to match those containing any new preparation). Furthermore the doctor also should, if possible, be unaware of which pills are which ; several investigations have shown that even the most well-intentioned clinicians can impart bias by their manner of asking questions and recording the answers. A trial in which the identity of two treatments is concealed from both the patient and the doctor is called "double-blind" ; this method should, if it is practicable, be used in any trial in which the assessments rely on opinion rather than fact. It is obvious that the patients should not all have the two drugs in the same order ; not only might the actual responses be governed by the order of administration but also it would be difficult to maintain the double-blind principle if the order was the same in each case. In this trial the key to the allocation of tablets was held in the Statistics Department (with a sealed copy in the Skin Department in case of emergency) ; this allocation was based on random numbers in such a way that, in the long run, an equal number of patients would have each type of tablet first.

The essential characteristic of a sequential trial is a specially constructed chart (shaped rather like an arrow-head) on which the results are recorded as they come in. When the graph crosses a boundary the trial stops, the results being judged "a significant difference" or "not a significant difference" according to which boundary was reached. In the itching trial only eleven preferences were needed (of which ten were for the active drug) before the boundary was crossed indicating a significant result—the conclusion being that the new drug did offer a real relief of the patient's symptoms.

I have described this trial in some detail ; apart from its being an example of a relatively new method of investigation it illustrates several points likely to be of importance in any trial. But in fact no two trials are alike ; in some investigations ethical considerations may play more of a part than in the trial just described ; in some there may be several criteria (some objective and some subjective). Other trials (not sequential) in which the Statistics Department has taken part in recent

years, have included one to compare an oral with an injected penicillin in the treatment of boils, and one to compare the rates of recovery from two short-term anaesthetics ; in the latter the criterion analysed was the ability to trace some lines and make a simple drawing.

#### *Surveys*

Clinical trials are the most spectacular, and possibly the most rewarding, application of medical statistics. But in some ways they are the simplest. Once the planning and organisation is complete the amount of analysis and calculation necessary may be trivial (this is particularly true in a sequential trial). Part of this simplicity usually arises from the fact that in a clinical trial the investigator has only a few definite questions to answer. In direct contrast to this is the "survey"—a word I will use to cover enquiries in which the investigator has no control over the factors he is studying. He collects data relating to a number of cases of a particular disease (it may be 20 or it may be 2,000) and tries to find out what light, if any, such data may shed on the aetiology, diagnosis and prognosis of the disease. The number of questions asked is potentially almost infinite. A survey may be retrospective—that is to say, based on records already in existence when the investigation starts, or it may be prospective—based on data collected specifically for the investigation. Generally speaking the prospective method is to be preferred if only for the reason that clinical notes are seldom complete ; items of information, such as physical signs, which the investigator may consider of importance in the study of the disease in general, may have been thought irrelevant in the case of the particular patient (or may have been missed through carelessness). In a prospective study the investigator has some control over the collection of his data.

An example of a prospective survey is one now being carried out in association with the Department of Bacteriology and the Casualty Department ; this is designed to find out something about staphylococcal infection. Swabs are taken from boils and septic wounds of patients attending the casualty department and from the noses of these and other patients. The patients are asked various questions about recent medical treatment (including antibiotics) and whether any of their families have recently been in hospital. The answers to these questions, together with the relevant

bacteriological data, are recorded on punched cards in the Statistics Department.\* These will enable us to relate, for example, the acquisition of resistant strains to previous medical history. Another prospective enquiry carried out in recent years was one designed to test whether there was a hereditary factor in lactational failure.

When time for research is limited it is inevitable that many investigations must be retrospective. The physician or surgeon studying a relatively rare condition may not be able to collect enough cases of his own; or the purpose of his investigation may be to find out the results of other people's methods of diagnosis or treatment. At this level the "survey" is simply an extension of the oldest of all methods of advancement of knowledge—learning by the experience of others. If it is worth studying other people's results it is worth studying them methodically. The investigator who ploughs through 500 notes, abstracts them and has them recorded and analysed by means of punched cards, will seldom "prove" anything about a disease in the sense, for example, of discovering a causal relationship between a method of treatment and its response, but he may well learn a great deal about the disease. Even if he only learns what are the questions that really need asking he will have taken a step forward.

#### *Cancer follow-up*

There is little that need be said about such

\* We use the Hollerith System, in which a card, measuring about 3 in. by 7 in., is punched with holes in such a way as to record, for instance, the results of 80 questions, each with 12 possible answers. The cards can be mechanically sorted and counted (by means of what Miss Hector calls our "iron piano").

surveys that we have been associated with, but it may be of interest to conclude this article with a short description of a project, partly prospective and partly retrospective, which is by far the most extensive of any that we have undertaken. Every year about a thousand cases of cancer are seen in the hospital. The Follow-up Department (whose activities were described some years ago in a *Journal* article) records such basic facts about each of these patients as their age, sex, diagnosis and method of treatment, and keeps in touch with them as long as they survive either by arranging that they should visit the hospital periodically or by writing to their general practitioners. This system began in 1947, so that by now that are records of more than 10,000 cases of malignant disease, half of whom have been followed up for five years or more. This survey is prospective in that the basic records are kept in accordance with a pre-arranged plan and that the machinery of the follow-up department ensures a coverage of 100 per cent, but is retrospective in that much of the details must still be dug out of the notes in the same way as in all the other retrospective trials I have mentioned. At present we are preparing, with the co-operation of various members of the staff, a Report which will show the five-year survival pattern of patients seen in the five years 1948-52. This is a task of considerable complexity, but the work, when completed, should provide a useful measure of the success of various forms of cancer treatment and a base-line from which to assess the value of the newer methods now being brought into use.

## Letters to the Editor

### THE MERITS OF A SCIENTIFIC EDUCATION

Dear Sir,

A recent editorial in this *Journal* (February, 1960) raises an interesting question which affects the opinion we have of ourselves as doctors and as persons supposedly qualified to be authoritative, often on matters outside clinical medicine. I refer to the conflict between The Arts and The Sciences, a problem which in many ways concerned our grandfathers more than ourselves, although in thinking circles in our time it causes

difficulty. In the first place, the methods of science are different from those of the humanites, so each way of thought should be applied in a different sphere; each gives an alternative solution to the thinker's query, unless his thought, like that of Socrates, embraces both. Herein lay the intellectual strength of the Greek culture, and much of its weakness also; for this thought-process breeds generality in philosophy to the extent that no answer is forthcoming to the lay-

man's question, so that the man in the street loses confidence in his intellectual superior. Nowadays, people label this way of thought "academic" in a disparaging tone. In the second place, the "arts brain" is found in a different kind of person from he who has a "scientific mind," and it is not as usual as it ought to be for each to choose a friend with the other. Those who have argued all night with historians and Greats students will, I think, understand this feeling.

An (Oxford) historian remarked to a physicist friend during one of those undergraduate arguments, "Oh yes, but you aren't qualified to talk, because what sort of education is a scientific one anyhow." He was young, and unfortunately meant this remark, because, like many artists he did not comprehend the scope of science. It is my belief that the study of Natural Philosophy is the finest training of the mind. At most schools, Sixth Form scientists, because of the danger of specialisation, are made to attend classes on subjects like Musical Appreciation, the History of Science, Art Appreciation, Ancient and Modern Literature and Modern Languages, all of which is right and useful, because it brings young scientists into contact with arts ideals and people. Many undergraduate scientists, however, have a grievance that the reverse does not occur in school to the arts Sixth-formers, who remain ignorant of the real meaning of scientific method unless they are lucky or clever enough to find out for themselves. Teaching the properties of salt is not to be compared with making a boy digest a large chunk of literature, and this

represents the sort of scientific knowledge that many arts students have when they take their degrees. They should be taught epistemology, say the scientists, and relativity and about stars and the Philosophy of Science. These are the things of which the universe is made and the things which can bind us all together under one philosophy, they say, and certainly any student who thinks in terms of the universal significance of these parts of science will have a broad outlook. They represent the greatest intellectual advances of our age, and it is for this reason that philosophers such as Russell and Whitehead have spent so much time and paper writing about them.

It is for this reason, too, that a good scientist will have a coherent system of thought into which he can fit most of his problems. The complaint is often made that this kind of education does not fit a person to deal with other people or to express himself to them, and this is true; but these abilities have more to do with the personal qualities of the thinker than his approach. Nevertheless, it is little use having a brilliant mind if it remains locked behind the doors of incoherence. This is especially true for the doctor. It is my view that neither the arts nor the sciences equip a man for self-expression, and this lack can only be rectified by something altogether outside formal education. If one's schooling trains one to use the mind, it has been effective.

Yours sincerely,

C. W. BURKE.

Abernethian Room.

## WASP STINGS

Dear Sir,

I was interested to read, in your February issue, Dr. Castleden's article on wasp stings, and the variable reactions so produced.

Whilst keeping wicket for the Southend Doctors' Cricket Club last season, a colleague of mine was stung three times in the course of one over by a wasp that had secreted itself in his "box." The only reaction in this instance was the passage of twelve byes.

The Cricket Club present an annual trophy for the most outstanding performance on the field of play, and my colleague has been nominated for this merit award.

The only other nominee, to date, is a student, borrowed for a needle match, who, in demonstrating his agility in the field, lost his glass eye. The ensuing search by the two teams, umpires and spectators, wasted sufficient time to save the Club from an ignominious defeat.

## LADIES' HOCKEY TEAM

Dear Sir,

An account of the Hospitals' Final for the Women's Hockey Shield will doubtless, in due course, appear in your columns, but I thought it might not be out of place to draw additional attention to the remarkable nature of the achievements of the Women's Hockey Club. Since 1954 the Hospitals' Shield has been won consecutively by the Bart's team, a remarkable series of victories apparently unrivalled in the history of all sports clubs in this Hospital. All honour is due to the nucleus of women students who have made this record possible, and in the face of most formidable opposition from schools carrying a far heavier proportion of feminine hockey talent. For the seventh successive year the Shield has come back to the College, having been wrested from vigorous competitors with a determined grace and elegance that must command the admiration of all Bart's supporters—*Ad multos annos!*

Yours sincerely,

MICHAEL J. BLUNT.

c/o The Westminster Bank Ltd.,  
High Street, Guildford.

The outcome of this interesting presentation is awaited expectantly by both medical and cricketing communities alike.

Yours sincerely,  
W. R. HUNT.

81 Kings Road,  
Westcliff-on-Sea,  
Essex.

### APPRECIATION AT LAST

Dear Sir,

May I begin this letter in the New Year by congratulating you and your recent predecessor, as Editors of the *Journal*, on a first-class job well executed. The *Journal* is awaited eagerly by myself, and each time read with satisfaction. May I call your attention to my present address, and express the hope that any Bart's men in the area will drop in. May I add that after one week in this place I met one of the nursing staff from P.Pott who had worked with me when I was a budding houseman! (Joan Featherstone). We had a truly overseas Bart's natter.



*Bart's Nurse*

In addition, may I thank your predecessor for inflating my ego by considering my articles on St. Bartholomew as "authoritative," but I hope you can enlist someone to go on from where I left off, as the subject was fascinating.

Yours sincerely,  
JOHN B. DAWSON.

University House  
Australian National University,  
Canberra, A.C.T.  
Australia.

Dear Editor,

I thought the last number of the Bart's *Journal* most excellent—it has encouraged me to renew my subscription. I had begun to wonder whether it was worth going on with it. All success in 1960.

Yours sincerely,  
AUBREY WESTLAKE.

Fordingbridge,  
Hants.

This letter refers to the November issue.—*Editor.*



*George's Nurse*

### MEMORIAL WINDOWS

Mr. F. C. Pitts, of Streatham, has written to the Editor pointing out that the nurse in the memorial window in the Church of St. Bartholomew-the-Less is a twin of the girl in the famous memorial window in Westminster Abbey. The twin, he says, has the same air of dedication and devotion and is, to all appearances, the same woman.

Mr. Pitts questioned the designer, Mr.

Hugh Easton, on this matter. Mr. Easton said that he had designed both windows but made separate drawings for each, one at Bart's and one at St. George's. There are, he says, "small differences between them." Mr. Easton added, "it just goes to show that good-looking nurses in uniform are not easy to tell apart."

## Sports News

### LADIES' HOCKEY

#### United Hospitals' Hockey Cup Final

On Saturday, March 5th, there met once again on the Middlesex ground at Chislehurst, the hockey teams of Bart's and the Royal Free Hospital, to do battle for the United Hospitals' trophy.

Both teams were rather nervous, and the standard of play was not of the best. At first the play was on the left, and Miss Swallow, just recovered from 'flu and playing in her seventh Cup Final, was hard worked.

The first goal was against the Hospital, being scored by the left inner in the Royal Free team. Play continued evenly and, just before half time, the Royal Free defence allowed a ball to run off her foot into the goal. So, at half time, the score was 1-1.

After the interval, Bart's were playing downhill and, after several corners, there came one from which Jennifer Hartley scored a fine goal, putting Bart's ahead. All efforts were now concentrated on resisting the very many attacks on the Bart's goal made by the Royal Free forwards.

Eventually the final whistle blew and Bart's had retained the trophy for the seventh successive year. The Shield was presented by Mr. Nash, the President of the U.H. Women's Hockey Club, to the Bart's captain, Elizabeth Knight. She thanked Mr. Nash for sparing his valuable time to watch the game and, then turning to the Bart's Club, she thanked the President, Prof. Wormall, and the three Vice-



*The team rests at half time*

Presidents, Dr. Blunt, Mr. Hume and Dr. Lehmann, who had all come to support the team. Finally, she thanked the opponents, the Royal Free Hospital, for making it such a good final.

## Book Reviews

### MIDWIFERY (A TEXTBOOK FOR PUPIL MIDWIVES)

by Garland & Perkes

Publishers : English Universities Press - Price 21s.

The authors of this book set out to produce a textbook of reasonable size and price, containing sufficient material to meet the requirements of the pupil midwife, and in this they have succeeded admirably.

The book is clear, well set out and up to date in its contents; the facts are presented fairly, conflicting viewpoints and their supportive evidence given with impartiality. The glossary is helpful in orientating the nurse to the language of obstetrics, while the proper names in heavier type make reference easier and also help to imprint them on the mind.

Illustrations are good, the clear line diagrams being easy to produce, with the exception of the foetal circulation (page 54) which may prove confusing since the atria are shown below the ventricles. The direction of vessels in the cord, and vessels to the liver might have been shown with advantage, giving insight into injection and replacement therapy by these routes.

Use of the metric system is a welcome innovation but the retention of the British Imperial System by its side is helpful.

The anatomy is perhaps a little on the brief side, but the physiology is clear particularly the menstrual cycle and the development and embedding of the ovum.

Chapters dealing with pregnancy, labour and the puerperium are clear and concise; abnormalities and their treatment simply explained with accent on aspects of particular interest to the midwife. Special tribute must be paid to their handling of ante partum haemorrhage and funic presentation and prolapse, no outmoded remedies having been suggested.

Although this book presupposes a background of General Training, there is much that would be useful to the "two yearly" pupil. The diseases associated with pregnancy such as cardiac and pulmonary conditions; and the section relating to rhesus incompatibility are simply explained and would be helpful in understanding certain alteration of treatment in these instances.

The normal and abnormal infant is clearly depicted and many modern trends given in this field. Finally the chapter on Social Services and Statutory Bodies is exceedingly useful for quick reference.

Altogether this is a book which can be thoroughly recommended to the nurse about to commence her midwifery training.

Miss R. E. Bailey,  
Midwife Teacher's Diploma.

**UROLOGY IN OUTLINE.** By T. L. Chapman, E. and S. Livingstone Ltd. pp. 176 27s. 6d.

The author in his preface to this first edition writes — "The presentation is somewhat unorthodox.

Most people carry information in their minds as successions of simple mental images" . . . and . . . "It is in the form of simple images that this introduction to urology is presented". Those drawings, to which the author refers, are very clear, lucidly portraying anatomical, pathological, physiological, embryological surgical and instrumental details. Each chapter is introduced by a short text followed by the drawings which adequately summarise the main points of the text.

An evening will suffice to read this book and the student will find it stimulating and consider it time well spent. Some students would appreciate more books, dealing with the subjects, written and illustrated in a similar vein.

**GENERAL PATHOLOGY AND BACTERIOLOGY FOR DENTAL STUDENTS** by Ronald L. Bishton, M.D. Published by John Wright, Bristol. Price 42s.

This well presented and illustrated book will certainly serve a need in the dental curriculum. It has excellent chapters on fundamentals, although "Inflammation" should surely come early in these basic first ten chapters. Staining procedures are deliberately omitted, but culture methods receive considerable space. Venepuncture, described in some detail, is omitted from the index, which does, however, score in incorporating the illustration figure numbers. Leucoplakia of the tongue would appear to be the only wise choice of the sole six coloured plates. As the book is written primarily for Dental Students, more stress could possibly have been given to dental aspects of disease, this would increase its undoubted value to students and practitioners.

**A BIOCHEMICAL APPROACH TO PATHOLOGY** by M. J. R. Dawkins and K. R. Rees. Published by Edward Arnold Ltd., 1959. 128 pp. Price 18/-.

Attempts have recently been made to correlate the morbid anatomical findings in disease with variations in the biochemical behaviour of cells from the normal. It will be seen from this book that the subject is still in its infancy, but some very interesting observations have already been made. The first chapter summarises in a simple manner the biochemistry necessary to understand the subsequent contents of the book. This is followed by a chapter on the submicroscopic organisation of the cell which in itself is not difficult to understand, but which is not generally taught in medical biochemistry. The authors then discuss the effects of toxic agents on the cells of the body, deficiency states, metabolic disorders and conclude with a chapter on the biochemistry of cancer. The book is too small for much detailed discussion to be possible, but the current theories are presented from an original viewpoint. The reader who is interested in the causes of certain diseases, rather than their appearance, will find this book stimulating, but its value is rather limited by the almost complete absence of references and the statements remain opinions of the authors rather than verifiable facts.

J.C.C.

**HAEMATOLOGICAL TECHNIQUE** by E. M. Darmady and S. G. T. Davenport. Published by J. and A. Churchill Ltd. 1958. Second edition. Price 24s.

This book is designed for the use of laboratory technicians working for the examination in Haema-



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tology and Blood Transfusion of the I.M.L.T., and also for the practical aspect of the same subjects relating to the senior medical student. This second edition includes a number of additional techniques, e.g. the investigation of the haemorrhagic disorders, the electrophoresis of haemoglobins and the Rose-Waaler test. Sections on blood bank organisation and parasitology present in the first edition have been omitted, but there are four new chapters on blood groups, serological and cross-matching work and blood transfusion reactions.

The text is clear and precise, and the great asset of the book is the collection and presentation, in a single volume of reasonable size, of much haematological data and techniques available otherwise only in more specialised manuals. At the close of many of the chapters are helpful brief lists of references, and there is also a glossary of terms at the end of the book. Constructive criticism is the absence of reference to the photo-electric cell for haemoglobin estimation, now the method of choice and certainly the most accurate. Other omissions are directions for preparing Coombs' reagent and also some general information and points on the significance of vitamin B<sub>12</sub> serum estimations and absorption tests.

The book undoubtedly fulfils the function which the authors had in mind, and its practical value as a bench book in the subject is established.

H.F.B.

#### BOOKS RECEIVED

*Textbook of Gynaecology*, by J. H. Peel. Published by Heinemann. Price 30s.

*Childbirth Without Fear*, by Grantley Dick-Reed. Published by Heinemann. Price 12s. 6d.

*Medical Terminology for Radiographers*, by P. M. Davies. Published by Heinemann. Price 15s.

*Principles of Pharmacology*, by J. J. Lewis. Published by Livingstone. Price 55s.

*Diagnosis in Locomotor Disorders*, by K. Stone. Published by O.U.P. Price 25s.

*Roy. Nat. Hosp. for Rheumatic Diseases, Bath. Reports*, Volume 10, 1958-59.

*Varicose Veins*, by T. Cleave. Published by John Wright & Sons. Price 7s. 6d.

*Clinical Physiology*, by E. J. M. Campbell and C. J. Dickinson. Published by Blackwell. Price 50s.

*Body Fluids in Surgery*, by A. W. Wilkinson. Published by Livingstone. Price 21s.

*A Final Study in the Nature of Disease*, by J. E. R. McDonagh. Published by Heinemann. Price 30s.

*An Introduction to Congenital Heart Disease*, by L. Schamroth and F. Segal. Published by Blackwell. Price 22s. 6d.

*Acknowledgement in this column does not preclude a review.*

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